

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

# REQUEST FOR ACCESS TO AN ABANDONED APPLICATION UNDER 37 CFR 1.14

Bring completed form to:  
File Information Unit  
Crystal Plaza Three, Room 1200  
2021 South Clark Place  
Arlington, VA  
Telephone: (703) 305-2733

**RECEIVED**  
**APR 14 2004**  
**File Information Unit**

In re Application of  
S, 532, 101 Queen  
Application Number 07/310252 Filed Feb 13, 1989  
Paper No. #32

I hereby request access under 37 CFR 1.14(a)(1)(IV) to the application file record of the above-identified ABANDONED application, which is identified in, or to which a benefit is claimed, in the following document (as shown in the attachment):

United States Patent Application Publication No. 5530101, page, \_\_\_\_\_ line \_\_\_\_\_  
United States Patent Number \_\_\_\_\_, column, \_\_\_\_\_, line, \_\_\_\_\_ or \_\_\_\_\_  
WIPO Pub. No. \_\_\_\_\_, page \_\_\_\_\_, line \_\_\_\_\_

## Related Information about Access to Pending Applications (37 CFR 1.14):

Direct access to pending applications is not available to the public but copies may be available and may be purchased from the Office of Public Records upon payment of the appropriate fee (37 CFR 1.19(b)), as follows:  
For published applications that are still pending, a member of the public may obtain a copy of:

- the file contents;
- the pending application as originally filed; or
- any document in the file of the pending application.

For unpublished applications that are still pending:

- (1) If the benefit of the pending application is claimed under 35 U.S.C. 119(e), 120, 121, or 365 in another application that has: (a) issued as a U.S. patent, or (b) published as a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:  
the file contents;  
the pending application as originally filed; or  
any document in the file of the pending application.
- (2) If the application is incorporated by reference or otherwise identified in a U.S. patent, a statutory invention registration, a U.S. patent application publication, or an international patent application publication in accordance with PCT Article 21(2), a member of the public may obtain a copy of:  
the pending application as originally filed.

John Icklan  
Signature

4/14/04  
Date

John Icklan  
Typed or printed name

Registration Number, if applicable  
202-297-8500  
Telephone Number

**RECEIVED**  
Approved APR 14 2004  
(Initials) [Signature]  
Unit **File Information Unit**

## [54] HUMANIZED IMMUNOGLOBULINS

[75] Inventors: Cary L. Queen, Los Altos; Harold E. Selick, Belmont, both of Calif.

[73] Assignee: Protein Design Labs, Inc., Mountain View, Calif.

[21] Appl. No.: 634,278

[22] Filed: Dec. 19, 1990

## Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 590,274, Sep. 28, 1990, abandoned, and a continuation-in-part of Ser. No. 310,252, Feb. 13, 1989, abandoned, which is a continuation-in-part of Ser. No. 290,975, Dec. 28, 1988, abandoned.

[51] Int. Cl.<sup>6</sup> ..... A61K 39/395; C07K 16/28

[52] U.S. Cl. .... 530/387.3; 530/387.1; 530/388.22; 424/133.1; 424/143.1

[58] Field of Search ..... 424/85.8, 133.1, 424/143.1; 530/387, 388.22, 387.1, 387.3

## [56] References Cited

## U.S. PATENT DOCUMENTS

4,816,397	3/1989	Boss et al.	435/68
4,816,567	3/1989	Cabilly et al.	530/387
4,867,973	9/1989	Geers et al.	
5,225,539	7/1993	Winter	

## FOREIGN PATENT DOCUMENTS

0171496	2/1986	European Pat. Off.
0173494	3/1986	European Pat. Off.
0184187	6/1986	European Pat. Off.
0239400	9/1987	European Pat. Off.
0266663	6/1988	European Pat. Off.
2188941	10/1987	United Kingdom
WO86/05513	9/1986	WIPO
WO87/02671	5/1987	WIPO
WO89/01783	3/1989	WIPO

## OTHER PUBLICATIONS

Vitteta et al., "Redesigning Nature's Poisons to Create Anti-Tumor Reagents," *Science* 238:1098-1104 (1987).  
Ellison et al., "The nucleotide sequence of a human immunoglobulin C(gamma)<sub>1</sub> gene", *Nucleic Acids Res.* 10:4071-(1982).Hieter et al., "Cloned Human and Mouse Kappa Immunoglobulin Constant and J Region Genes Conserve homology in Functional Segments", *Cell* 22:197-207 (1980).Sharon et al., "Expression of a V<sub>H</sub>C<sub>K</sub> chimaeric protein in mouse myeloma cells", *Nature* 309:364-367 (1984).Takeda et al., "Construction of chimaeric processed immunoglobulin genes containing mouse variable and human constant region sequences", *Nature* 314:452-454 (1985).Tan et al., "A Human-Mouse Chimeric Immunoglobulin Gene with a Human Variable Region is Expressed in Mouse Myeloma Cells", *J. Immunol.* 135:3564-3567 (1985).Morrison et al., "Chimeric human antibody molecules: Mouse antigen-binding domains with human constant region domains," *Proc. Natl. Acad. Sci.* 81:6851-6859 (1984).Boulianne et al., "Production of functional chimeric mouse/human antibody," *Nature* 312:643-646 (1984).Neuberger et al., "A hapten-specific chimeric IgE antibody with human physiological effector function," *Nature* 314:268-270 (1985).Morrison, S. L., "Transfectomas Provide Novel Chimeric Antibodies," *Science* 229:1202-1207 (1985).Sahagan et al., "A Genetically Engineered Murine/Human Chimeric Antibody Retains Specificity for Human Tumor-Associated Antigen", *J. Immunol.* 137:1066-1074 (1986).Liu et al., "Expression of mouse:human immunoglobulin heavy-chain cDNA in lymphoid cells", *Gene* 54:33-40 (1987).Better et al., "Escherichia coli Secretion of an Active Chimeric Antibody Fragment", *Science* 240:1041-1043 (1988).Waldmann, T. A., "The Structure, Function, and Expression of Interleukin-2 Receptors on Normal and Malignant Lymphocytes," *Science* 232:727-732 (1986).Leonard et al., "The human receptor for T-cell growth factor," *J. Biol. Chem.* 260:1872-1880 (1985).Farrar, J., "The biochemistry, biology, and role of interleukin-2 in the induction of cytotoxic T cell and antibody-forming B cell receptors," *Immunol. Rev.* 63:129-166 (1982).Greene et al., "Growth of Human T Lymphocytes: An Analysis of Interleukin 2 and Its Cellular receptor", in *Progress in Hematology XIV*, E. Brown ed., Grune and Statton, New York (1986) pp. 283-301.Verhoyen et al., "Reshaping Human Antibodies: Grafting an Antilysozyme Activity", *Science* 239:1534-1536 (1988).Jones et al., "Replacing the complementarity-determining regions in a human antibody with those from a mouse", *Nature* 321:522-525 (1986).Hale et al., "Remission Induction in Non-Hodgkin Lymphoma with Reshaped Human Monoclonal Antibody CAMPATH-1H", *Lancet* Dec. 17, 1988, pp. 1394-1399.Chothia, C. and A. M. Lesk, "Canonical Structures for the Hypervariable Regions of Immunoglobulins", *J. Mol. Biol.* 196:901-917 (1987).

(List continued on next page.)

Primary Examiner—Lila Feisee

Attorney, Agent, or Firm—Townsend and Townsend and Crew

[57]

## ABSTRACT

Novel methods for producing, and compositions of, humanized immunoglobulins having one or more complementarity determining regions (CDR's) and possible additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided. Each humanized immunoglobulin chain will usually comprise, in addition to the CDR's, amino acids from the donor immunoglobulin framework that are, e.g., capable of interacting with the CDR's to effect binding affinity, such as one or more amino acids which are immediately adjacent to a CDR in the donor immunoglobulin or those within about 3 Å as predicted by molecular modeling. The heavy and light chains may each be designed by using any one or all of various position criteria. When combined into an intact antibody, the humanized immunoglobulins of the present invention will be substantially non-immunogenic in humans and retain substantially the same affinity as the donor immunoglobulin to the antigen, such as a protein or other compound containing an epitope.